GRAND ROUNDS in Environmental Medicine

HARVARD MEDICAL SCHOOL AND
BOSTON MEDICAL CENTER

Violence: An Unrecognized Environmental Exposure that May Contribute to Greater Asthma Morbidity in High Risk Inner-City Populations

Rosalind J. Wright and Suzanne F. Steinbach

[1]Beth Israel Deaconess Medical Center, Pulmonary and Critical Care Division and the Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; [2]Department of Pediatrics, Boston Medical Center, Boston, Massachusetts, USA

In the United States, rising trends in asthma prevalence and severity, which disproportionately impact minorities and the urban poor, have not been fully explained by traditional physical environmental risk factors. Exigencies of inner-city living can increase psychosocial risk factors (e.g., stress) that confer increased asthma morbidity. In the United States, chronic exposure to violence is a unique stressor existing in many high-risk urban neighborhoods. In this paper, we describe a series of cases that exemplify a temporal association between exposure to violence and the precipitation of asthma exacerbations in four urban pediatric patients. In the first three cases, the nature of the exposure is characterized by the proximity to violence, which ranged from direct victimization (through either the threat of physical assault or actual assault) to learning of the death of a peer. The fourth case characterizes a scenario in which a child was exposed to severe parental conflict (i.e., domestic violence) in the hospital setting. Increasingly, studies have begun to explore the effect of living in a violent environment, with a chronic pervasive atmosphere of fear and the perceived or real threat of violence, on health outcomes in population-based studies. Violence exposure may contribute to environmental demands that tax both the individual and the communities in which they live to impact the inner-city asthma burden. At the individual level, intervention strategies aimed to reduce violence exposure, to reduce stress, or to counsel victims or witnesses to violence may be complementary to more traditional asthma treatment in these populations. Change in policies that address the social, economic, and political factors that contribute to crime and violence in urban America may have broader impact. ***Key words*****: asthma, case series, inner-city, stress, violence.** ***Environ Health Perspect*** **109:1085–1089 (2001). [Online 2 October 2001]** ***http://ehpnet1.niehs.nih.gov/docs/2001/109p1089-1089wright/abstract.html***

Case Presentation

We present three cases encountered in the Boston City Hospital Pediatric Allergy–Immunology–Respiratory Clinic and a fourth case seen as an inpatient at Boston City Hospital in which exposure to violence seemed to be the asthma symptom precipitant.

Case 1. Case 1 is a 12-year-old African-American girl with lifelong asthma who has numerous recognized triggers that include pollen, cold air, and exercise. She had presented several times each year to her neighborhood clinic with acute wheezing that responded to nebulized bronchodilator treatment. On initial evaluation in July 1994, her physical exam was notable for allergic rhinitis. Pulmonary function testing showed a mild obstructive defect primarily affecting the small airways: forced vital capacity (FVC), 94%; forced expiratory volume in 1 sec (FEV_1), 79%; and forced expiratory flow rate over the middle 50% of the FVC volume ($FEF_{25\%–75\%}$), 51%. Oral antihistamines, nasal cromolyn, and inhaled steroids were added to her inhaled bronchodilator therapy. In the subsequent month, amoxicillin was begun for sinusitis, and nasal steroids were added to her treatment regimen. After a period of symptom stability she developed increased wheezing in October 1994. Oral prednisone was begun, resulting in rapid improvement to her baseline by the fifth day which was Halloween. On Halloween night, the patient heard gunshots outside of her home in a housing project and shortly thereafter became aware that one of her peers had been fatally shot. She quickly developed recurrent wheezing, slept poorly that night due to respiratory symptoms, and required an extended course of prednisone to control the recurrent asthma exacerbation. Following recovery from this episode, her asthma stabilized.

Case 2. Case 2 is a 15-year-old Hispanic girl who has had severe asthma since infancy and is now enrolled in a college preparatory course in an urban high school. Her history was remarkable because of her need for assisted ventilation with status asthmaticus at the age of 2 years and subsequent every-other-day prednisone therapy up to the age of 5 years. Her currently recognized asthma triggers include exercise, upper respiratory tract infections, and exposure to dust and pets. Allergy skin testing demonstrated sensitivities to several environmental allergens. She was controlled on theophylline, inhaled serevent, flunisolide, nedocromil, oral antihistamines, and regular peak flow monitoring. Typical pulmonary function test results before and after bronchodilator therapy, respectively, in the Pediatric Allergy–Immunology–Respiratory clinic for this patient were FVC, 68% and 100%, FEV_1, 43% and 69%, and $FEF_{25\%–75\%}$, 17% and 31%. During the fall of 1994 she developed increased wheezing on three occasions, which required pulse doses of prednisone. Each episode began on a Sunday evening before the start of a new school week. Inquiry revealed that, at the end of the previous school year, the girl had been attacked on a subway platform by a group of girls. She was physically attacked and her jewelry and book bag, containing her asthma medications, were stolen. In retrospect, Case 2 reported an acute asthma episode immediately after the assault. The patient later identified the assailants to the police and pressed charges against them. Through the fall, the patient encountered her assailants periodically on the subway. She subsequently experienced an asthma flare after a court appearance where she testified against her attackers; during this court appearance, they verbally threatened her. After the sentencing of the assailants, the patient had no further

Address correspondence to R.J. Wright, Channing Laboratory, 181 Longwood Avenue, Boston, MA USA 02115. Telephone: (617) 525-0867. Fax: (617) 525-0958. E-mail: rosalind.wright@channing.harvard.edu

R.J.W. received support from NIH training grant HL07427 and the Medical Foundation Deborah Munroe Noonan Memorial Fund.

Received 24 April 2001; accepted 20 July 2001.

documented acute asthma exacerbations for 15 months corresponding to the period of incarceration of her assailants. Over this time course she stopped taking her medications except for an albuterol inhaler as needed and she did not receive follow-up in the Pediatric Allergy-Immunology-Respiratory Clinic. Following the release of the assailants, she again developed severe symptoms requiring two hospitalizations in a 2-month period.

Case 3. Case 3 is a 9-year-old Caucasian girl with asthma since early infancy. The known triggers include exercise, emotional upsets, and upper respiratory tract infections. Allergy skin testing demonstrated sensitivity to many environmental allergens including *Aspergillus*. Sputum cultures have been repeatedly negative for *Aspergillus*, and measured immunoglobulin E (IgE) is 154. Her asthma was managed on inhaled flunisolide, cromolyn, an albuterol inhaler as needed, nasal cromolyn, and diphenhydramine. During the spring of 1994, frequent asthma exacerbations led to a 3-month course of prednisone. Typical pulmonary function test results were as follows: FVC, 90%; FEV_1, 69%; and $FEF_{25\%–75\%}$, 41%. Intensive allergen control measures in the home, including replacing carpeting with linoleum, installing a dehumidifier, restoring crumbling walls, and fumigation, were associated with success in weaning the patient off prednisone and normalization of her spirometry. In October 1994 her daily wheezing returned. It was subsequently revealed that Case 3 had been assaulted on the school bus by an older boy and had reported the incident to teachers. Thereafter the perpetrator's female cousin began to threaten to stab the patient with sharp scissors while they were riding the school bus. The patient finally refused to board the school bus one day for the ride home and subsequently developed wheezing and respiratory distress requiring emergency treatment.

Case 4. Case 4 is a 3-year-old girl admitted to the pediatric intensive care unit (ICU) with an asthma exacerbation in the setting of a viral illness and an exposure to sprayed pesticide 10 days before the onset of symptoms. The patient's initial oxygen saturation was 77% on room air and 89–95% on a 100% non-rebreather face mask. She did not require intubation. Three days into her hospital course, the patient began to show slow clinical improvement on a medical regimen that included continuous nebulized ventolin treatments, intravenous solumedrol, ipratroprium bromide nebulized treatments, and a continuous terbutaline infusion, which was started on the second hospital day.

Case 4's mother stayed with her around the clock. Visits by the patient's father were associated with loud arguments between the parents, which were overheard by the medical staff caring for the patient. On one occasion, a nurse observed the patient's mother slapping the father and then the patient's father pushing and shoving the mother. The health care staff noted that the patient's respiratory rate had increased from 50–60 breaths/min to 80–90 breaths/min during her exposure to these parental encounters. One event documented in the medical record describes the father hitting the mother, causing her to crash into the glass doors of the patient's ICU room. The patient became visibly upset and began screaming. Vital signs documented before the event charted a respiratory rate of 30–34 breaths/min, a heart rate of 145 beats/min, a temperature of 99.4°F, and oxygen saturation of 92% on a 40% face mask. Vital signs documented in the 3–4 hr after the episode showed a clinical decompensation with a respiratory rate of 42–50 breaths/min, a heart rate of 155–180 beats/min, and an initial oxygen saturation of 91% on a 70% face mask. A clinical exam documented decreased air movement and recurrent wheezing associated with the persistent tachypnea and tachycardia.

Discussion

These cases exemplify a temporal association between exposure to violence and the precipitation of asthma exacerbations in four inner-city pediatric patients. Although each patient is vulnerable to a variety of asthma triggers, exposure to violent events seemed to be a common precipitant of asthma symptoms. Notably, Case 2 experienced improvement in her chronic asthma symptoms once the perceived threat of violence was no longer present and deterioration in her respiratory status when that threat reemerged. In Case 4, there was a clear temporal association between witnessing parental conflict and deterioration in the patient's clinical course and vital signs. Because of a raised awareness, we are now inquiring about exposure to violence as an apparent asthma symptom precipitant. Although these cases support a role of exposure to violence and acute exacerbations of established asthma, we should also consider plausible pathways through which living in a violent environment may influence the genesis of asthma.

Asthma is the most common chronic disease of childhood and a leading cause of morbidity in children. In the United States, recent trends of increasing childhood asthma prevalence and morbidity disproportionately affect nonwhite children living in urban areas and children living in poverty (*1–3*). It is not clear that differences in generally known asthma risk factors such as chemical and particulate air pollutants (*4*), environmental and *in utero* tobacco smoke exposure (*5*), viral respiratory infections (*6*), and home allergen exposure (*7*) fully explain these trends. As yet unidentified unique factors may contribute to the higher asthma morbidity and mortality rates seen in inner-city poor minority populations (*8*).

Connections between the health and economic well-being of populations are increasingly seen to be embedded within the larger context of people's lives. It has been proposed that differential exposure to and perception of stress may, in part, explain socioeconomic disparities in health (*9*). Various sociodemographic characteristics (e.g., lower social class, ethnic minority status) may predispose individuals to particular pervasive forms of life stress (*10,11*), and the degree of chronic stress can be significantly influenced by the characteristics of the communities in which people live (*12*). Chronic stress in U.S. urban populations has been conceptualized as neighborhood disadvantage, characterized by the presence of a number of community-level stressors including poverty, unemployment, substandard housing, and high crime/violence rates (*13*). Such physical and social factors can be a source of environmental demands that contribute to stress experienced by populations living in a particular area (*14*).

Studies in minority and lower-income populations have shown a high prevalence of children who encounter violence in the inner city. A prevalence study at Boston City Hospital found that 10% of children had witnessed a knifing or shooting before the age of 6 years; 18% had witnessed shoving, kicking, or punching; and 47% had heard gunshots (*15*). In an inner-city cohort in Chicago, Illinois, investigators found that of children between the ages of 7 and 13, 42% had seen someone shot and 37% had seen someone stabbed (*16*). A survey of urban elementary school children in New Orleans, Louisiana, found that more than 90% had witnessed violent episodes, 70% involving use of weapons (*17*). Although stress is decidedly common and has many causes in our society, the increased prevalence of chronic community violence is a specific and extreme stressor confronting the urban poor.

Violence can be conceptualized as a source of psychological and environmental stress that taxes both the individual and the communities in which they live. Community violence can be considered a pervasive stressor that adds to environmental demands imposed on an already vulnerable population of children and families (*18*). Inner-city populations that experience high rates of exposure to violence are also characterized by high levels of poverty, hopelessness, lack of opportunity, and unemployment (i.e., chronic ongoing stressors). Living in a violent environment is

associated with a chronic pervasive atmosphere of fear and the perceived threat of violence (*19,20*). Children and families living with community violence are likely to view their world and their lives as being out of their control. Facing daily life experiences in an unpredictable or uncontrollable environment predisposes these populations to greater deleterious effects of stress (*21*). Moreover, both the duration and the frequency of experienced stress are important determinants of its impact on health and illness. Variable response to acute challenges (e.g., high frequency of exposure to violence) superimposed on chronic stressors (e.g., other components of neighborhood disadvantage) may have different implications on disease expression (*22*). Events that last a very short time can also have more long-term stress effects through lasting physiologic responses thought to be maintained by recurrent unwanted or "intrusive" thoughts about past events (*23*). Symptoms of post-traumatic stress disorder (PTSD), including flashbacks or recurrent memories of traumatic events, are highly associated with exposure to violence (*24*).

Psychological stress has been associated with the activation of the hypothalamic–pituitary–adrenal (HPA) axis and disturbed regulation of the HPA system.This may best be understood within McEwen el al.'s concept of allostasis, which refers to the ability of the body to achieve stability through change, such that "the autonomic nervous system, the HPA axis, and cardiovascular, metabolic, and immune systems protect the body by responding to internal and external stress" (*25*). The potential cost of such accommodation is conceptualized as allostatic load, which is the wear and tear from chronic overactivity (or underactivity) of the HPA system. With regard to immune function, during a period of acute stress, increased cortisol and catecholamines promote allostasis by influencing cell trafficking and by modulating cytokines, which fight infection (*26*). In contrast, chronic overactivity (or underactivity) of these same mediators may result in allostatic load (i.e., potential immunosuppressive effects when the mediators are chronically secreted or not turned off). Some optimal level of mediators is needed to maintain a functional balance, and the absence of appropriate levels of gluccocorticoids and catecholamines may allow other immune mediators to overreact and increase the risk of inflammatory disorders (*27*). In this framework, violence can be conceptualized as a psychosocial environmental exposure that can "get into the body" and result in biological changes that may contribute to asthma morbidity.

There is a renewed interest in the links between psychological stimuli and asthma (*28,29*). Exposure to violence as a major life stressor may impact on the pathogenesis of asthma and/or contribute to the morbidity of disease by triggering exacerbations through neuroimmunologic mechanisms. Augmented parasympathetic response has been documented after intense or prolonged stress experiences (*30,31*). Increased parasympathetic tone produces increased smooth muscle tone in the lung and thus may mediate emotionally induced bronchoconstriction in asthma (*32*). Cytokines known to be important in inflammatory diseases like asthma may also serve a role in mediating the acute response to physical and emotional stress. Psychosocial stressors can moderate both humoral and cellular immune function (*33,34*). Stressor-linked alterations in the immune system may predispose to respiratory tract infections (*35,36*), which may trigger acute asthma exacerbations. Stress hormones influence immunoglobulin and cytokine expression and thus may increase a genetically predisposed individual's risk of developing asthma. Current knowledge supports the notion that expression of the asthmatic phenotype, as related to the immune response, is modulated by environmental factors that include viral infection, air pollutants, maternal smoking, breast-feeding, and allergen exposure (*37*). Stress may potentiate the allergic response to allergens by increasing the release of inflammatory mediators and the subsequent cascade of inflammatory events characteristic of chronic asthma. That is, violence as a psychosocial stressor may be an "adjuvant" to the asthmatic inflammatory response. Thus, while stress and emotional distress are generally recognized as factors aggravating asthma symptoms in those with existing disease, they may play a role in the genesis of the disease as well (*29*).

Preliminary empirical evidence suggests that exposure to violence may contribute to the burden of asthma morbidity on the inner-city poor. In a cohort study in Boston, Wright et al. (*38*) retrospectively ascertained lifetime exposure to violence through a parental-report interview questionnaire administered to 416 caregivers and their children who are being followed longitudinally for respiratory health outcomes, including asthma. Preliminary analyses suggest a link between higher lifetime exposure to community violence and an increased risk of asthma and wheeze syndromes and prescription bronchodilator use.

Violence exposure may ameliorate resources needed to manage and cope with chronic asthma. Exposure to community violence (and other determinants of neighborhood disadvantage) may operate through effects on impulse control, risk-taking behavior, and the adoption of coping behaviors such as smoking, thus leading to increased exposure to a known environmental asthma trigger (*39*). Smoking can be conceptualized, at the individual level, as a strategy to cope with negative affect or stress (*40,41*). Neighborhood effects on health behaviors such as smoking have also been demonstrated (*42,43*). For example, evidence from the 1987 General Social Survey (*44*) suggests that stress may be one factor promoting increased prevalence of smoking in African-American communities. Romano et al. (*45*) surveyed 1,137 African-American households and found that the strongest predictor of smoking was a report of high-level stress, represented by a "hassles" index. The "hassles" index was an abbreviated 10-item scale based on items chosen to represent a dimension that community residents involved in the project perceived to be especially relevant. Notably, among the items were neighborhood level factors including being concerned about violence or living in an unsafe area.

Community-level characteristics such as increased prevalence of violence may influence an individual's behavior, resulting in increased exposure to other known environmental risk factors for asthma. Parents in high-violence communities may restrict their children's outdoor activities. In the same Boston pediatric cohort discussed above, parental reports of keeping children indoors primarily because of fear of neighborhood violence was related to increased risk of wheeze and physician's diagnosis of asthma prior to the age of 2 years (*46*). Reasonable hypotheses as to why this association was seen may include the following. The child who is kept indoors may become deconditioned, experiencing shortness of breath with decreasing levels of exertion. An increased sedentary lifestyle may be linked to obesity in children. Recent studies have linked obesity to asthma (*47,48*), and studies suggest that obesity has increased among families living in poverty in the United States (*49*). Also, children who are kept indoors may be exposed for longer periods to indoor aeroallergens and have an increased likelihood of sensitization and allergic symptoms in response to dust mite, pet, roach, and rodent allergens. Parents who are worried about their children's safety in their neighborhood because of crime may keep their children indoors and otherwise restrict their social behavior; thus each child's ability to develop support networks may be compromised (i.e., exposure to violence may lead to diminished stress-buffering factors such as social networks) (*50*). Psychopathology (e.g., PTSD, depression) influenced by life stress and chronic exposure to violence may also prevent the child from forming relationships that are necessary to promote normal social development. Fear of crime fosters a distrust of

others and can contribute to social isolation (*51*). It is clear that violence is related to factors that limit formation of social networks. These additional supports may be especially important to health and well-being in high-risk urban populations faced with cumulative effects of many other ecologic stressors (i.e., poverty, low education, poor housing).

Coping with a violent environment may affect compliance with therapy and medical follow-up for asthma. Fong (*52*) discussed the impact of violence on the management of hypertensive urban African Americans, underscoring violence as a perceived barrier to keeping appointments and following prescribed exercise programs. Fear of making a trip across town to a pharmacy or medical facility or adhering to a prescribed walking program as a result of prior victimization or a perceived threat of violence may be a barrier to compliance. This may lead to lapses in use of prophylactic medication, delayed intervention, and consequently greater morbidity. Adolescents who witness violence are more likely to develop a foreshortened sense of the future (*53*) and thus a fatalistic outlook that may undermine their ability to invest in the future by complying with a chronic asthma treatment regimen. Other barriers to adherence to a prescribed asthma regimen may include the lack of a community pharmacy open 24 hr/day. Pharmacies may be reluctant to remain open 24 hr/day in poor communities, especially when violence is a concern. Violence can indirectly affect access to medical care by diverting limited funds away from primary care and specialty clinics, including those caring for asthmatics (*54,55*).

Exposure to violence may affect asthma management when increased family dysfunction impedes development of appropriate coping strategies necessary to facilitate improved quality of care for the asthmatic child. Dysfunctional patterns are common in homes of children with asthma and may be precipitated by anxiety experienced around asthmatic attacks (*56*). Family dysfunction has been related to increased asthma morbidity and mortality (*57,58*). The level of stress in the home of an asthmatic child is likely to increase as parents attempt to balance the child's need for activity and independence with their concerns about avoiding allergen- or exercise-induced symptoms and maintaining adherence to a pharmacologic regimen. Likewise, stress and anxiety may be compounded in families who are also faced with the real or perceived threat of violence or injury in the child's home, neighborhood, or school, which leads to greater dysfunction. Parents who have experienced violence, or whose children have had such experiences, may develop depression or PTSD, which impairs their ability to supervise and respond to their children. This reduction in parenting capacity may undermine an adult's ability to coordinate a child's ongoing asthma care.

Conclusions

Exigencies of inner-city living, such as coping with the high prevalence of exposure to violence, may increase psychosocial risk factors, which in turn may confer increased asthma morbidity on high-risk urban populations. High crime rates, and thus the real or perceived threat of violence, are specific aspects of the inner-city environment that may impact psychologic functioning as well as health-promoting and health care-seeking behaviors of the inhabitants (*59*). More research is needed to examine the public health impact of children and their families living with violence. Systematic exploration of an association between violence (an urban stressor) and asthma throughout childhood may help us to understand the rise in asthma prevalence, severity, and medical care use as well as to further our understanding of its disproportionate occurrence in poor urban children in this country. We present these cases to alert clinicians and researchers to a potential risk factor for increased asthma morbidity that has not previously been recognized.

Increasingly, pediatricians are being asked to manage chronic childhood illness in the context of complicated family and community environments that clearly impact disease management. Pediatricians have long recognized the impact of violence on the health and well-being of children and have been expanding efforts to increase response to exposure to violence as a health care issue in the clinical setting (*60*). The identification of exposure to violence as a trigger of asthma exacerbations may alert health professionals caring for asthmatics in the inner-city setting to inquire about patient's exposure among other known triggers. Secondary intervention strategies designed to reduce exposure to violence or to facilitate positive coping mechanisms for individual patients may obviate the need for more aggressive and costly pharmacologic therapies for asthma with potential side effects. For example, referral to a stress reduction program or to programs that provide counseling for children who have witnessed or experienced violence (*61*) may be helpful. In our experience, it is unlikely that the child's asthma control can be improved unless such psychosocial issues are also addressed.

Primary prevention at the population or neighborhood level should also be considered. Social cohesion and social capital are strongly correlated with rates of violent crime within neighborhoods (*62*). Research suggests that crime is most prevalent in societies that permit large disparities in the material standards of living of its citizens, which in turn are created by broad-scale societal and political factors (*63,64*). Emerging evidence underscores the need for policy makers to pay increased attention to political and economic forces that result in further marginalization of minority populations in the inner city and contribute to the growing income gap between the rich and the poor in this country (*65*). Policies aimed at improvements in life opportunities and living conditions may increase social cohesion and decrease violence in the inner cities. Social cohesion may influence the health behaviors of neighborhood residents by promoting diffusion of health information or increasing the adoption of healthy behaviors through exerting social control over smoking. Improved neighborhood social capital may impact health through increased access to local services and amenities (e.g., safe transportation, pharmacy availability). It is unlikely that the health problems of disadvantaged populations can be solved unless we try to understand the potential role of unique environmental stressors such as violence exposure.

References and Notes

1. Gergen PH, Weiss KB. Changing patterns of asthma hospitalization among children: 1979 to 1987. JAMA 264:1688–1692 (1990).
2. Mannino DM, Homa DM, Pertowski CA, Ashizawa A, Nixon LL, Johnson CA, Ball LB, Jack E, Kang DS. Surveillance for Asthma—United States, 1960–1995. Morb Mortal Wkly Rep CDC Surveill Summ 47:1–27 (1998).
3. Wright RJ, Weiss ST. Epidemiology of allergic disease. In: Allergy (Holgate ST, Church M, Lichtenstein LM, eds). 2nd ed. London:Mosby, 2000;203–212.
4. Braun-Fahrlander C, Ackermann-Liebrich V, Schwartz J, Gnehm HP, Rutishauser M, Wanner HM. Air pollution and respiratory symptoms in preschool children. Am Rev Respir Dis 145:42–47 (1992).
5. Martinez FD, Cline M, Burrows B. Increased incidence of asthma in children of smoking mothers. Pediatrics 89:21–26 (1992).
6. Busse WE, Gern JE, Dick EC. The role of respiratory viruses in asthma. In: The Rising Trends in Asthma (Chadwick DJ, Cardew G, eds). Ciba Foundation Symposium 206. West Sussex, England. Chichester, England/New York:John Wiley & Sons, Ltd, 1997;208–219.
7. Sporik R, Holgate ST, Platts-Mills TA, Cogswell JJ. Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood: a prospective study. N Engl J Med 323:502–507 (1990).
8. Weiss KB, Gergen PJ, Crain EF. Inner-city asthma: the epidemiology of an emerging U.S. public health concern. Chest 101:362S–367S (1992).
9. Adler N, Boyce T, Chesney M, Cohen S, Folkman S, Kahn R, Syme SL. Socioeconomic status and health: the challenge of the gradient. Am Psychol 49:15–24 (1994).
10. Rabkin JG, Struening EL. Life events, stress and illness. Science 194:1013–1020 (1976).
11. Dohrenwend BP, Dohrenwend BS, eds. Social status and psychological disorder. New York:John Wiley, 1969.
12. Taylor SE, Repetti RL, Seeman T. Health psychology: what is an unhealthy envrionment and how does it get under the skin? Annu Rev Psychol 48:411–447 (1997).
13. Attar BK, Guerra NG, Tolan PH. Neighborhood disadvantage, stressful life events and adjustment in urban elementary-school children. J Clin Child Psychol 23:391–400 (1994).
14. Evans GW. Environmental stress and health. In: Handbook of Health Psychology (Baum A, Revenson TA, Singer JE,

eds). Mahwah, NJ:Lawrence Erlbaum Associates, Inc., 2001;365–385.
15. Taylor L, Zuckerman B, Harik V, McAlister-Groves B. Witnessing violence by young children and their mothers. J Dev Behav Pediatr 15:120–123 (1994).
16. Sheehan KM, DiCara JA, LeBailly S, Christoffel KK. Children's exposure to violence in an urban setting. Arch Pediatr Adolesc Med 151(5):502–504 (1997).
17. Osofsky JD, Wewers S, Hann DM, Fick AC. Chronic community violence: what is happening to our children? Psychiatry 56:36–45 (1993).
18. Isaacs MR. Violence: The Impact of Community Violence on African American Children and Families. Arlington, VA:National Center for Education in Maternal and Child Health, 1992.
19. Herman AA. Political violence, health, and health services in South Africa. Am J Public Health 8:767–768 (1988).
20. Zapata BC, Rebolledo A, Atalah E, Newman B, King MC. The influence of social and political violence on the risk of pregnancy complications. Am J Public Health 82:685–690 (1992).
21. Cohen S, Kessler RC, Underwood Gordon L, eds. Strategies for measuring stress in studies of psychiatric and physical disorders. In: Measuring Stress: A Guide for Health and Social Scientists. New York:Oxford University Press, 1995;3–26.
22. Pike JL, Smith TL, Hauger RL, Nicassio PM, Patterson TL, McClintock J, Costlow C, Irwin MR. Chronic life stress alters sympathetic, neuroendocrine, and immune responsivity to an acute psychological stressor in humans. Psychosom Med 59:447–457 (1997).
23. Baum A. Stress, intrusive imagery, and chronic distress. Health Psychol 9:653–675 (1990).
24. Fitzpatrick KM, Boldizar JP. The prevalence and consequences of exposure to violence among African-American youth. J Am Acad Child Adolesc Psychiatry 32:424–430 (1993).
25. McEwen BS, Biron CA, Brunson KW, Bulloch WH, Chambers WH, Dhabhar FS, Goldfarb RH, Kitson RP, Miller AH, Spencer RL, et al. The role of adrenocorticoids as modulators of immune function in health and disease: neural, endocrine, and immune interactions. Brain Res Rev 23:79–133 (1997).
26. Brosschot JF, Benschop RJ, Godaert GLR, Olff M, DeSmef M, Heimen CJ, Ballieux RF. Influence of life stress on immunological reactivity to mild psychological stress. Psychosom Med 56:216–224 (1994).
27. Sternberg EM. Neural-immune interactions in health and disease. J Clin Invest 100:2641–2647 (1997).
28. Busse WE, Kiecolt-Glaser JK, Coe C, Martin RJ, Weiss ST, Parker SR. Stress and asthma: NHLBI Workshop Summary. Am J Respir Crit Care Med 151:249–252 (1994).
29. Wright RJ, Rodriguez M, Cohen S. Review of psychosocial stress and asthma: an integrated biopsychosocial approach. Thorax 53:1066–1074 (1998).
30. Gelhorn E. The neruophysiological basis of anxiety: a hypothesis. Perspect Biol Med 8:488–505 (1965).
31. Vingerhoets AJM. The role of the parasympathetic division of the autonomic nervous system in stress and the emotions. Int J Psychosom 32:28–34 (1985).
32. Nadel JA, Barnes PJ. Autonomic regulation of the airways. Ann Rev Med 35:451–467 (1984).
33. Kiecolt-Glaser JK, Glaser R. Psychosocial moderators of immune function. Ann Behav Med 9:16–20 (1987).
34. Kiecolt-Glaser JK, Glaser, R. Stress and immune function in humans. In: R. Psychoneuroimmunology II (Ader R, Felten D, Cohen N, eds). San Diego, CA:Academic Press, 1991;849–867.
35. Cohen S, Tyrell DAJ, Smith AP. Psychological stress and susceptibility to the common cold. N Eng J Med 325:606–612 (1991).
36. Graham NMH, Douglas RB, Ryan P. Stress and acute respiratory infection. Am J Epidemiol 124:389–401 (1986).
37. Donovan CE, Finn PW. Immune mechanisms of childhood asthma. Thorax 54:938–946 (1999).
38. Wright RJ, Hanrahan JP, Tager I, Speizer F. Effect of the exposure to violence on the occurrence and severity of childhood asthma in an inner-city population [Abstract]. Am J Respir Crit Care Med 155:A972 (1997).
39. Barker RG. Habitats, Environments, and Human Behavior. San Francisco:Jossey-Bass, 1978.
40. Beckham JC, Roodman AA, Shipley RH, Hetzberg MA, Cunha GH, Kudler HS, Levin ED, Rose JE, Fairbank JA. Smoking in Vietnam combat veterans with posttraumatic stress disorder. J Trauma Stress 8:461–472 (1995).
41. Acierno R, Kilpatrick DG, Resnick HS, Saund CL. Violent assault, posttraumatic stress disorder, and depression: risk factors for cigarette use among adult women. Behav Modif 20:363–384 (1996).
42. Kleinschmidt I, Hills M, Elliott P. Smoking behavior can be predicted by neighborhood deprivation measures. J Epidemiol Comm Health 87:1113–1118 (1997).
43. Reijneveld S. The impact of individual and area characteristics on urban socioeconomic differences in health and smoking. Int J Epidemiol 27:33–40 (1998).
44. Feigelman W, Gorman B. Toward explaining the higher incidence of cigarette smoking among black Americans. J Psychoact Drugs 21:299–305 (1989).
45. Romano PS, Bloom J, Syme SL. Smoking, social support, and hassles in an urban African-American Community. Am J Public Health 81:1415–1422 (1991).
46. Wright RJ, Speizer FE, Tager I, Hanrahan JP. Children's distress and violence exposure: relation to respiratory symptoms, asthma, and behavior [Abstract]. Am J Respir Crit Care Med 157:A41 (1998).
47. Camargo CA Jr, Field AE, Colditz GA, Speizer FE. Body mass index and asthma in children age 9–14 [Abstract]. Am J Respir Crit Care Med 159:A150 (1999).
48. Stenius-Aarniala B, Poussa T, Kvarnstrom J, Gronlund EL, Ylikahri M, Mustajoki P. Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. Br Med J 320:827–832 (2000).
49. Gortmacher SL, Must A, Sobol AM, Peterson K, Colditz GA, Dietz WH. Television viewing as a cause of increasing obesity among children in the United States, 1986–1990. Arch Pediatr Adolesc Med 150:356–362 (1996).
50. Sampson RJ. Family management and child development: insights from social disorganization theory. In: Facts, Frameworks, and Forecasts: Advances in Criminological Theory (McCord J, ed). New Brunswick, NJ:Transaction Publishers,1992;63–93.
51. Krause N. Stress and isolation form close ties in later life. J Gerontol 46:S183–194 (1992).
52. Fong RL. Violence as a barrier to compliance for the hypertensive urban African-American. J Natl Med Assoc 87:203–207 (1995).
53. Augustyn MS, Parker B, McAlister-Groves B, Zuckerman B. Silent victims: children who witness violence. Contemp Pediatr 12:35–57 (1995).
54. Fleming AW, Sterling-Scott RP, Carabello G, Imari-Williams I, Allmond B, Foster RS, Kennedy F, Shoemaker WC. Injury and violence in Los Angeles: impact on access to health care and surgical education. Arch Surg 127:671–676 (1992).
55. Robicsek R, Ribbeck B, Walker LG. The cost of violence: the economy of health care delivery for non-accidental trauma in an urban southeastern community. NC Med J 54:578–582 (1993).
56. Gustafsson PA, Kjeillman IM, Ludvigsson J, Cederblad M. Asthma and family interaction. Arch Dis Child 62:258–263 (1987).
57. Boxer GH, Carson J, Miller BD. Neglect contributing to tertiary hospitalization in childhood asthma. Child Abuse Negl 12:491–501 (1988).
58. Strunk RC, Mrazek DA, Fuhrmann GS, LaBrecque JF. Physiologic and psychological characteristics associated with deaths due to asthma in childhood. A case-controlled study. JAMA 254:1193–1198 (1985).
59. Kauffman KS. Center as haven: findings of an urban ethnography. Nurs Res 44:231–236 (1995).
60. Stringham P. Violence anticipatory guidance. Pediatr Clin N Am 2:439 (1998).
61. Grove B. The child witness to violence project. Disch Plann Update 14:14–18 (1994).
62. Sampson RJ, Raudenbush SW, Earls F. Neighborhoods and violent crime: a multilevel study of collective efficacy. Science 277:918–924 (1997).
63. Kawachi I, Kennedy BP, Wilkinson RG. Crime: social disorganization and relative deprivation. Soc Sci Med 48:719–731 (1999).
64. Wallace D, Wallace R. Scales of geography, time, and population: the study of violence as a public health problem. Am J Public Health 88:1853–1858 (1998).
65. Kawachi I, Kennedy BP. Income inequality and health: pathways and mechanisms. Health Serv Res 34:215–227 (1999).